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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/510,001	09/30/2004	Masayuki Amagai	4439-4025	3825

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EXAMINER	
GAMBEL, PHILLIP	

ART UNIT	PAPER NUMBER
1644	

NOTIFICATION DATE	DELIVERY MODE
12/24/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/510,001	AMAGAI ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed 09/11/2008, has been entered.

Claims 1 and 3 have been amended.

For the record, it is noted that while applicant submits that support for the newly amended claims can be found throughout the specification, including Example 2,
the only written support for the newly amended claims appear to be on page 1 of the instant specification (see Technical Field).

Claims 1 and 3 are pending and being acted upon in the instant application.

Claims 2 and 4 have been canceled previously.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Office Action.

This Office Action will be in response to applicant's amendment, filed 09/11/2008.

The rejections of record can be found in previous Office Action, mailed 06/12/2008.

3. Claims 3 is rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention essentially for the reasons of record.

Applicant's arguments, filed 09/11/2008, have been fully considered but have not been found convincing essentially for the reasons of record.

Applicant argues the following.

The Examiner contends that "[t]he problem here is that applicant has not provided direction in the application as-filed to teach the skilled artisan how to make and use the information that certain people were predisposed to pemphigus or to utilize anti-CD40L antibodies to prevent the reoccurrence of the disease." (Office Action - Page 3). However, applicants respectfully assert that this observation is inconsistent with the instant disclosure.

Applicants describe in the working Example, how "[t]he preventive effect on pemphigus by the administration of MR1 antibody [anti-CD40L antibody]" was examined and evaluated. (See Example 2 of the instant specification). Specifically, applicants "[e]xamined whether the transferred splenocytes were capable of inducing immunological tolerance to Dsg3 when MR1 antibody was preventively administered so that CD40L was present at the time of inducing immune response to Dsg3." (See Id, page 12).

[P]roduction of the anti-Dsg3 antibody was confirmed in the control group 14 days after the transfer, while any apparent antibody production or phenotype was not observed at all throughout the observation period of 66 days in the MR1- administered mice (Fig. 1). In addition, weight loss, hair loss in resting period and the immediate suprabasal acantholysis which is a pathohistological feature ofPV [pemphigus] was observed in the control group, whereas neither weight loss nor symptoms of PV [pemphigus] was observed in the MR1 [anti-CD40L] administered group. The MR1 antibody apparently showed a preventive effecton PV [pemphigus]." (See Id, page 12; emphasis added).

One skilled in the art, contrary to the Examiner's contention, would not and could not doubt that the applicants provide ample support for a preventive effect of MR1 (anti-CD40L) antibodies on pemphigus in the art-recognized mouse models of pemphigus onset. Applicants respectfully direct the Examiner's attention to Example 2, which describes the mouse model. However, the Examiner also questions the correlation of a mouse model to human diseases by alleging that "[w]ith respect to in vivo studies, animal models validate concepts based on studies of human disease, such studies are limited to the 'acute' as opposed to 'chronic' nature of the disease." (Office Action - page 4). However, applicants respectfully assert that such misguided observation by the Examiner could then be incorrectly made of evers~ single animal model ever developed and constitute a mere speculation. The court upheld Applicants' position that [a]n ... in vivo animal model example in the specification, in effect, constitutes a "working example" if that example "correlates" with a disclosed or claimed method invention.

In this regard, the issue of "correlation" is also dependent on the state of the prior art. In other words, if the art is such that a particular model is recognized as correlating to a specific condition, then it should be accepted as correlating unless the examiner has evidence that the model does not correlate. Even with such evidence, the examiner must weigh the evidence for and against correlation and decide whether one skilled in the art would accept the model as reasonably correlating to the condition. In re Brana, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995) (See MPEP 2164.02).

In fact, to demonstrate the preventive capabilities of the claimed invention, applicants describe the use of autoantigen-knockout mice, which are recognized in the art to represent an active autoimmune disease model for pemphigus (Amagai, et al. The Journal of Clinical Investigation 105(5):625-631, 2000; previously submitted). The Examiner is invited to provide any evidentiary support to demonstrate that this autoantigen-knockout mouse model would not in fact be recognized by one of ordinary skill in the art as a model for onset and progression of pemphigus, anything less than that is merely speculative. Furthermore, the Examiner states that the applicants have "... not sufficiently addressed the unpredictability and inconsistency of treating patients with pemphigus, as evidenced by The Merck Manual of Diagnosis and Therapy, Seventeenth Edition..." (Office Action - Page 3), and further states that according to the Merck Manual "[P]emphigus is a serious disease with an inconsistent and unpredictable response to therapy and that the aim of treatment is to stop the eruption of new lesions. See Treatment on page 829. Therefore, the treatment of pemphigus is drawn to the treatment of the disease and its associated lesions subsequent to an individual being diagnosed with pemphigus and not as a preventative agent of the disease itself, as recited in the current claims." (Office Action - page 4; emphasis added). Applicants respectfully disagree. Applicants assert that the claim 3 as presently amended is directed to preventing pemphigus in patients who are likely to suffer from recurrence (i. e., exacerbation) of pemphigus, which was successfully demonstrated in a working example 2 on a mouse-model of pemphigus. Hence, the description in the Merck Manual cited above (i. e., "...the aim of treatment is to stop the eruption of new lesions") is immaterial in the context of the claim because the Merck Manual concentrates on presently available treatments with steroids, which are dangerous and require such stringent guidelines as presented by the Examiner. Whereas, applicants have discovered a novel method of treatment and prevention of pemphigus based on a highly specific immunosuppressant therapy unrelated to the use of steroids. Thus, one skilled in the art would not apply the same guidelines as recited in the Merck Manual intended for the use with a non-specific immunosuppressant agents to a highly specific immunosuppressant therapy based on administering anti-CD40L antibodies of the present invention. Therefore, applicants assert that the reliance on the Merck Manual in the context of the current invention is misplaced.

For the reasons stated above, at the time of the invention, one skilled in the art, having read the instant specification, would understand that the claimed method of treating and preventing pemphigus would not necessitate undue experimentation to make and/or use the same, and would be fully enabled to practice the claimed invention. Reconsideration and withdrawal of the enablement rejection under 35 U.S.C. § 112, first paragraph are respectfully requested.

Although applicant indicates that Amagai et al., Journal of Clinical Investigation 105: 625-631,2000;

once again, it is noted that this reference does not appear in the current record.

In the interest of compact prosecution, the examiner is providing a copy for the record.

Here, in contrast to applicant's reliance upon the applicant's experimental animal model as a predictor of "preventing pemphigus" in human therapy,

Amagai et al. (Journal of Clinical Investigation 105: 625-631, 2000; notes that while the animal model is used for screening various therapeutic interventions, the animal model does not address the usual triggers of autoimmune diseases (e.g., see entire document, including the Discussion, particularly page 630, column 2, paragraph 2).

Furthermore, applicant's co-authored publication Aoki-Ota et al. (Journal of Investigative Dermatology 126: 105-113, 2006) notes that when anti-CD154 antibody was injected after the mice developed the pemphigus vulgaris phenotype, no significant suppression fo the proeuction of anti-Dsg3 IgG was observed and after stable production of pathogenic antibodies was established, anti-CD154 treatment had only marginal effects (see entire document, including the Abstract and Discussion).

Again, applicant has not sufficiently addressed the unpredictability and inconsistency of treating patients with pemphigus, as evidenced by The Merck Manual of Diagnosis and Therapy, Seventeenth Edition (edited by Beers et al., Merck Research Laboratories, Whitehouse Station, NJ, 1999; see pages 829-831) (892; of record) and reiterated below.

Also, with respect to animal models, applicant has not sufficiently addressed the following also of record and reiterated below.

Also, it is noted that experimental protocols usually are conducted under defined conditions wherein the antagonist and the stimulus / insult occur at the same or nearly the same time. Immunosuppression is much easier to achieve under such controlled conditions that experienced in the human disorders or diseases such as pemphigus targeted by the claimed "preventative agents". With respect to in vivo studies, animal models validate concepts based on studies of human disease, such studies are limited to the "acute" as opposed to "chronic" nature of the disease. In animal models, the onset of inflammation is rapid with an aggressive destructive process, whereas in humans the disease progresses more slowly, often with natural periods of disease exacerbation and remission. Generally, such diseases are diagnosed only after significant tissue damage has occurred.

The following is reiterated for applicant's convenience.

In vitro and animal model studies have not correlated well with in vivo clinical trial results in patients. Since the therapeutic indices of immunosuppressive drugs or biopharmaceutical drugs can be species- and model-dependent, it is not clear that reliance on the in vitro and in vivo experimental observations as well as the clinical experience with targeting various inflammatory conditions with CD40L- specific antibodies accurately reflects the relative ability or efficacy of the claimed "preventative agents" to prevent pemphigus.

Pharmaceutical therapies in the absence of in vivo clinical data are unpredictable for the following reasons; (1) the protein may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half-life of the protein; (2) the protein may not reach the target area because, i.e. the protein may not be able to cross the mucosa or the protein may be adsorbed by fluids, cells and tissues where the protein has no effect; and (3) other functional properties, known or unknown, may make the

protein unsuitable for in vivo therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

The specification does not adequately teach how to effectively prevent pemphigus by administering CD40L-specific antibodies / CD40L antagonists. The specification does not teach how to extrapolate data obtained from various in vitro or in vivo observations as well as clinical experience with CD40L-specific antibodies / CD40L antagonists to the development of effective methods of preventing pemphigus in humans broadly encompassed by the claimed invention.

Also, it is noted that experimental protocols usually are conducted under defined conditions wherein the antagonist and the stimulus / insult occur at the same or nearly the same time. Immunosuppression is much easier to achieve under such controlled conditions that experienced in the human disorders or diseases such as pemphigus targeted by the claimed "preventative agents". With respect to in vivo studies, animal models validate concepts based on studies of human disease, such studies are limited to the "acute" as opposed to "chronic" nature of the disease. In animal models, the onset of inflammation is rapid with an aggressive destructive process, whereas in humans the disease progresses more slowly, often with natural periods of disease exacerbation and remission. Generally, such diseases are diagnosed only after significant tissue damage has occurred.

For example, The Merck Manual of Diagnosis and Therapy, Seventeenth Edition (edited by Beers et al., Merck Research Laboratories, Whitehouse Station, NJ, 1999; see pages 829-831) indicates that:
Pemphigus is a serious disease with an inconsistent and unpredictable response to therapy and that the aim of treatment is to stop the eruption of new lesions.
See Treatment on page 829.
Therefore, the treatment of pemphigus is drawn to the treatment of the disease and its associated lesions subsequent to an individual being diagnosed with pemphigus and not as a preventative agent of the disease itself, as recited in the current claims.

There is insufficient guidance and direction as well as objective evidence to provide for preventing pemphigus recited in the instant claims.

In view of the lack of predictability of the art to which the invention pertains the lack of established clinical protocols for effective methods to prevent pemphigus with therapeutic agents, undue experimentation would be required to practice the claimed "preventative agents" to prevent pemphigus with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed "preventative agents" and absent working examples providing evidence which is reasonably predictive that the claimed "preventative agents" are effective for preventing pemphigus encompassed by the claimed products.

Applicant's arguments have not been found persuasive.

Again, applicant is invited to amend the claims to avoid the recitation of "preventing" as reading on keeping pemphigus recurrence from happening.

Also, as noted previously and addressed below,
for prior art examination purposes, there appears no manipulative differences between the prior art method steps and ingredients and the claimed methods.

Furthermore, the prior art teaching of treating pemphigus with anti-CD40L antibodies reads on treating and in turn, preventing pemphigus as it reads on preventing the eruption of new lesions in the long course of treatment of this disease (e.g., see pages 829-831, particularly Treatment).

4. Claims 1 and 3 are rejected under 35 U.S.C. § 102(b) as being anticipated by Black et al. (U.S. Patent No. 6,001,358) (see entire document) alone essentially for the reasons of record or in further evidence by The Merck Manual of Diagnosis and Therapy, Seventeenth Edition (edited by Beers et al., Merck Research Laboratories, Whitehouse Station, NJ, 1999; see pages 829-831) (892; or record) essentially for the reasons of record.

Applicant's arguments, filed 09/11/2008, have been fully considered but have not been found convincing essentially for the reasons of record.

Applicant argues the following.

As previously noted in the response of June 29, 2007, the '358 patent characterizes humanized antibodies to human gp39 (also called CD40L; Column 3, line 46) that could potentially be used to treat 141 autoimmune and non-autoimmune ailments where one of them happens to be pemphigus (para. bridging columns 32 and 33). The '358 patent provides no support for this assertion and lacks any examples (working or prophetic) of treatment of any disorder.

Applicants respectfully assert that the '358 patent in fact does not enable a method of using anti-CD40L antibody to treat or prevent pemphigus. The '358 patent discloses "a laundry list of diseases" that anti-CD40L antibody ~ treat, and offers only speculation that this compound might successfully treat pemphigus.

Applicants further assert that there is no evidence that a person of ordinary skill in the art would find that the '358 patent provides support for a treatment against pemphigus and the gaps in the '358 patent cannot be filled by extrinsic knowledge because no such extrinsic knowledge existed. Specifically, according to the background section of the '358 patent, anti-gp39 (anti-CD40L antibody) was hypothesized to potentially prevent CD40 signaling in B cells, thus inhibiting T-cell dependent antibody responses based on the finding that gp39-CD40 interactions are essential for antibody responses against thymus dependent antigens. (Col. 4, lines 30-44). Theses studies were based on animal models of collagen-induced arthritis and experimental allergic encephalomyelitis (multiple sclerosis) (Col. 4, lines 30-44; Col. 5, lines 21-39), not pemphigus. Neither one of these disease models is related to pemphigus, which represents a group of rare autoimmune mucocutaneous blistering disorders that are mediated by circulating immunoglobulin G (IgG) autoantibodies against the desmosomal cadherins (See page 1 of the instant specification). Applicants respectfully assert that the specification of the '358 patent does not provide an enabled disclosure that an anti-CD40L antibody can be used in the treatment of medical conditions associated with the effects of an autoimmune mucocutaneous blistering disorders. In fact, such disclosure creates "substantial uncertainty" regarding the use of CD40 signaling inhibiting T-cell dependent antibody response compounds in the treatment of pemphigus. The court held that the prior art reference in question is not enabled when a disclosure leaves "substantial uncertainty,". Elan Pharms., Inc. v. Mayo Found., 346 F.3d 1051, 1057 (Fed. Cir. 2003).

Therefore, applicants assert that the disclosure of the '358 patent is not enabled for treating or preventing pemphigus by administering anti-CD40L antibody as claimed and thus, as a matter of law, does not anticipate the claimed invention. Reconsideration and withdrawal of the § 102(b) rejection to claims 1 and 3 are respectfully requested.

Again, in contrast to applicant's assertions that the prior art does not disclose that the anti-CD40L antibody is effective in preventing pemphigus, does not provide experimental data and is an incomplete invention,

applicant is reminded that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See In re Casey, 152 USPQ 235 (CCPA 1967) and In re Otto, 136 USPQ 458, 459 (CCPA 1963). Also, see MPEP 2111.02

Products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01.

Also, it is noted that proof of efficacy is not required in order for prior art reference to be enabling for purposes of anticipation. See Impax Laboratories Inc. v. Aventis Pharmaceuticals Inc., 81 USPQ2d 1001 (Fed. Cir. 2006).

In contrast to applicant's arguments, the prior art does not leave "substantial uncertainty" for treating pemphigus with anti-CD40L antibodies.

Attorney argument cannot take the place the evidence lacking in the record. Meitzner v. Mindick, 193 USPQ 17, 22 (CCPA 1977).

Given the broadest reasonable interpretation of the claims, including preventing the development of pemphigus as reading on treating a patient with pemphigus or characteristics of pemphigus and preventing its further development, which is consistent with the instant specification (e.g., see page 3, paragraph 1 and the Disclosure of the Invention on pages 3-5 of the instant specification).

Also, given the broadest reasonable interpretation of the claims and the nature of treating pemphigus, which involves a long course of therapy which aims includes immediate and subsequent to stop the eruption of new lesions, as evidenced by the Merck Manual,

the prior art teaching of treating pemphigus with anti-CD40L antibodies reads on treating and in turn, preventing pemphigus as it reads on preventing the eruption of new lesions in the long course of treatment of this disease (e.g., see pages 829-831, particularly Treatment).

The following is reiterated for applicant's convenience.

Black et al. teach antagonistic anti-CD40L antibodies, including compositions thereof (e.g., see columns 34-38) as well as their use in the inhibition of CD40L:CD40- mediated interactions, including the treatment of autoimmune and non-autoimmune conditions (e.g., see columns 31-34), including pemphigus (e.g., see column 33, lines 4-5) (see entire document, including Summary of the Invention, Detailed Description of the Invention and Claims). Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced antagonistic anti-CD40L antibodies and therapeutic compositions thereof.

Applicant's arguments have not been found persuasive.

5. Claims 1 and 3 are rejected under 35 U.S.C. § 102(e) as being anticipated by Black et al. (U.S. Patent No. 7,122,187) (see entire document) alone
or in further evidence by The Merck Manual of Diagnosis and Therapy, Seventeenth Edition (edited by Beers et al., Merck Research Laboratories, Whitehouse Station, NJ, 1999; see pages 829-831) (892; of record) essentially for the reasons of record.

Applicant's arguments, filed 09/11/2008, have been fully considered but have not been found convincing essentially for the reasons of record and addressed above in the previous Section.

Applicant argues the following.

Applicants respectfully wish to direct the Examiner's attention to the fact that the '187 patent claims priority to the '358 patent discussed in the previous section. Applicants assert that there is no evidence that a person of ordinary skill in the art would find that the '358 patent provides support for a treatment ofpemphigus and the gaps in the '358 patent are not filled by the subsequent filing of the '187 patent. By the same token as discussed above in reference to the '358 patent, applicants assert that the '187 patent does not anticipate a method of using anti-CD40L antibody to treat or prevent pemphigus because the ' 187 patent just like its parent (the '358 patent) does not enable a person of ordinary skill in the art to treat pemphigus with anti-CD40L antibody.

Therefore, applicants assert that the ' 189 patent application is not enabled for treating or preventing pemphigus by administering anti-CD40L antibody and thus as a matter of law does not anticipate the claimed invention. Reconsideration and withdrawal of the § 102(e) rejection to claims 1 and 3 are respectfully requested.

Again, in contrast to applicant's assertions that the prior art does not disclose that the anti-CD40L antibody is effective in preventing pemphigus, does not provide experimental data and is an incomplete invention,
applicant is reminded that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See In re Casey, 152 USPQ 235 (CCPA 1967) and In re Otto, 136 USPQ 458, 459 (CCPA 1963). Also, see MPEP 2111.02

Products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01.

Here, applicant ignores the claims of Black et al. (U.S. Patent No. 6,001,358). U.S. patents are presumed valid by U.S. courts unless proven otherwise. See 35 U.S.C. 282.

Also, it is noted that proof of efficacy is not required in order for prior art reference to be enabling for purposes of anticipation. See Impax Laboratories Inc. v. Aventis Pharmaceuticals Inc., 81 USPQ2d 1001 (Fed. Cir. 2006).

In contrast to applicant's arguments, the prior art does not leave "substantial uncertainty" for treating pemphigus with anti-CD40L antibodies.

Attorney argument cannot take the place the evidence lacking in the record. Meitzner v. Mindick, 193 USPQ 17, 22 (CCPA 1977).

The following of record is reiterated for applicant's convenience.

Black et al. teach antagonistic anti-CD40L antibodies, including compositions thereof (e.g., see columns 34-38) as well as their use in the inhibition of CD40L:CD40- mediated interactions, including the treatment of autoimmune and non-autoimmune conditions (e.g., see columns 31-34), including pemphigus (e.g., see column 33, lines 4-5) (see entire document, including Summary of the Invention, Detailed Description of the Invention and Claims).

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced antagonistic anti-CD40L antibodies and therapeutic compositions thereof.

In addition to the teachings of Black et al. (U.S. Patent No. 6,001,358) of record and set forth above, Black et al. (U.S. Patent No. 7,122,187) has been added in that this patent includes claimed methods of treating pemphigus (e.g., see Claim 1).

U.S. patents are presumed valid by U.S. courts unless proven otherwise. See 35 U.S.C. 282.

Given the broadest reasonable interpretation of the claims, including preventing the development of pemphigus as reading on treating a patient with pemphigus or characteristics of pemphigus and preventing its further development, which is consistent with the instant specification (e.g., see page 3, paragraph 1 and the Disclosure of the Invention on pages 3-5 of the instant specification).

Also, given the broadest reasonable interpretation of the claims and the nature of treating pemphigus, which involves a long course of therapy which aims includes immediate and subsequent to stop the eruption of new lesions, as evidenced by the Merck Manual,
the prior art teaching of treating pemphigus with anti-CD40L antibodies reads on treating and in turn, preventing pemphigus as it reads on preventing the eruption of new lesions in the long course of treatment of this disease (e.g., see pages 829-830, particularly Treatment).

Applicant's arguments have not been found persuasive.

6. Claims 1 and 3 are rejected under 35 U.S.C. § 102(e) as being anticipated by Di Padova et al. (US 2004/0038293 A1) (see entire document) alone

or in further evidence by The Merck Manual of Diagnosis and Therapy, Seventeenth Edition (edited by Beers et al., Merck Research Laboratories, Whitehouse Station, NJ, 1999; see pages 829-831) (892; of record) essentially for the reasons of record.

Applicant's arguments, filed 09/11/2008, have been fully considered but have not been found convincing essentially for the reasons of record and addressed above in the previous Section.

Applicant argues the following.

By the same token as discussed above in reference to the '358 patent, the '293 application similarly discloses "a laundry list of diseases" that CD154 (anti-CD40L antibody) treat (approximately 140 different disorders listed; See para. [0083]), and offers only speculation that this compound might successfully treat pemphigus. Therefore, applicants assert that the '293 application in fact does not anticipate a method of using anti-CD40L antibody to treat or prevent pemphigus because the '293 application does not enable a person of ordinary skill in the art to treat or prevent pemphigus with anti-CD40L antibody. In fact, the '293 application merely speculates on the subject without any support of extrinsic knowledge. The Examiner is invited to provide evidentiary support to demonstrate that a person of skill in the art would find that the '293 application is enabling for a treatment against pemphigus. Similarly to the '358 patent, the '293 application does not adequately provide an enabling disclosure that anti-CD40L antibody can be used in the treatment of medical conditions associated with the effects of autoimmune mucocutaneous blistering disorders and creates "substantial uncertainty" regarding use of CD40 signaling inhibiting T-cell dependent antibody response compounds in the treatment of pemphigus. The court held that the prior art reference in question is not enabled when a disclosure leaves "substantial uncertainty,". Elan Pharms., Inc. v. Mayo Found., 346 F.3d 1051, 1057 (Fed. Cir. 2003).

Again, in contrast to applicant's assertions that the prior art does not disclose that the anti-CD40L antibody is effective in preventing pemphigus, does not provide experimental data and is an incomplete invention,

applicant is reminded that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See In re Casey, 152 USPQ 235 (CCPA 1967) and In re Otto, 136 USPQ 458, 459 (CCPA 1963). Also, see MPEP 2111.02

Products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01.

Here, applicant ignores the claims of Di Padova et al. (U.S. Patent No. 6,001,358). U.S. patents are presumed valid by U.S. courts unless proven otherwise. See 35 U.S.C. 282.

Also, it is noted that proof of efficacy is not required in order for prior art reference to be enabling for purposes of anticipation. See Impax Laboratories Inc. v. Aventis Pharmaceuticals Inc., 81 USPQ2d 1001 (Fed. Cir. 2006).

In contrast to applicant's arguments, the prior art does not leave "substantial uncertainty" for treating pemphigus with anti-CD40L antibodies.

Attorney argument cannot take the place the evidence lacking in the record. Meitzner v. Mindick, 193 USPQ 17, 22 (CCPA 1977).

The following of record is reiterated for applicant's convenience.

Di Padova teach antagonistic anti-CD40L antibodies, including compositions thereof (e.g., see paragraphs [0086] and [0090] – [0091]) as well as their use in the inhibition of CD40L:CD40- mediated interactions (see entire document), including the treatment of autoimmune and non-autoimmune conditions (e.g., see paragraphs [0081] – [0101], including pemphigus (e.g., see paragraph [0083] and Claim 10) (see entire document, including Claims).

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced antagonistic anti-CD40L antibodies and therapeutic compositions thereof in their treatment of pemphigus.

Given the broadest reasonable interpretation of the claims, including preventing the development of pemphigus as reading on treating a patient with pemphigus or characteristics of pemphigus and preventing its further development, which is consistent with the instant specification (e.g., see page 3, paragraph 1 and the Disclosure of the Invention on pages 3-5 of the instant specification).

Given the broadest reasonable interpretation of the claims, including preventing the development of pemphigus as reading on treating a patient with pemphigus or characteristics of pemphigus and preventing its further development, which is consistent with the instant specification (e.g., see page 3, paragraph 1 and the Disclosure of the Invention on pages 3-5 of the instant specification).

Also, given the broadest reasonable interpretation of the claims and the nature of treating pemphigus, which involves a long course of therapy which aims includes immediate and subsequent to stop the eruption of new lesions, as evidenced by the Merck Manual,
the prior art teaching of treating pemphigus with anti-CD40L antibodies reads on treating and in turn, preventing pemphigus as it reads on preventing the eruption of new lesions in the long course of treatment of this disease (e.g., see pages 829-831, particularly Treatment).

It is noted that Di Padova et al. also teaches "treatment and/or prevention diseases or disorders" (e.g., see paragraph [0083]).

7. Claim 3 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Black et al. (U.S. Patent No. 7,122,187) OR Di Padova et al. (US 2004/0038293 A1) in view of The Merck Manual of Diagnosis and Therapy, Seventeenth Edition (edited by Beers et al., Merck Research Laboratories, Whitehouse Station, NJ, 1999; see pages 829-831) (892; of record) essentially for the reasons of record.

Applicant's arguments, filed 09/11/2008, have been fully considered but have not been found convincing essentially for the reasons of record and addressed above in the previous Section.

Applicant argues the following.

Applicants assert that the combination of the '187 patent or the '293 application with the Merck Manual does not teach, disclose, or suggest the method of preventing pemphigus using anti-CD40 antibodies. Specifically, applicants respectfully assert that the Merck Manual does not cure the deficiencies of either the '187 patent or the '293 application noted in the previous subsections, i.e., lack of enablement for treatment of pemphigus using anti-CD40 antibodies. Thus, applicants contend, that the proposed combination of references fails to teach, disclose, or suggest all of the elements of applicants' claims. For at least these reasons, reconsideration and withdrawal of the rejections under 35 U.S.C. § 103 (a) of the claim 3 are respectfully requested.

Again, in contrast to applicant's assertions that the prior art does not disclose that the anti-CD40L antibody is effective in preventing pemphigus, does not provide experimental data and is an incomplete invention,

applicant is reminded that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See In re Casey, 152 USPQ 235 (CCPA 1967) and In re Otto, 136 USPQ 458, 459 (CCPA 1963). Also, see MPEP 2111.02

Products of identical chemical composition cannot have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01.

Here, applicant ignores the claims of Di Padova et al. (U.S. Patent No. 6,001,358). U.S. patents are presumed valid by U.S. courts unless proven otherwise. See 35 U.S.C. 282.

Also, it is noted that proof of efficacy is not required in order for prior art reference to be enabling for purposes of anticipation. See Impax Laboratories Inc. v. Aventis Pharmaceuticals Inc., 81 USPQ2d 1001 (Fed. Cir. 2006).

In contrast to applicant's arguments, the prior art does not leave "substantial uncertainty" for treating pemphigus with anti-CD40L antibodies.

Attorney argument cannot take the place the evidence lacking in the record. Meitzner v. Mindick, 193 USPQ 17, 22 (CCPA 1977).

The following of record is reiterated for applicant's convenience

Given applicant's arguments concerning the recitation of "preventing pemphigus",
This obviousness rejection has been set forth as it reads on the broadest reasonable interpretation of the claims and to address applicant's arguments.

Black et al. teach antagonistic anti-CD40L antibodies, including compositions thereof (e.g., see columns 34-38) as well as their use in the inhibition of CD40L:CD40- mediated interactions, including the treatment of autoimmune and non-autoimmune conditions (e.g., see columns 31-34), including pemphigus (e.g., see column 33, lines 4-5) (see entire document, including Summary of the Invention, Detailed Description of the Invention and Claims).

Di Padova teach antagonistic anti-CD40L antibodies, including compositions thereof (e.g., see paragraphs [0086] and [0090] – [0091]) as well as their use in the inhibition of CD40L:CD40- mediated interactions (see entire document), including the treatment of autoimmune and non-autoimmune conditions (e.g., see paragraphs [0081] – [0101], including pemphigus (e.g., see paragraph [0083] and Claim 10) (see entire document, including Claims).

Given the broadest reasonable interpretation of the claims, including preventing the development of pemphigus as reading on treating a patient with pemphigus or characteristics of pemphigus and preventing its further development, which is consistent with the instant specification (e.g., see page 3, paragraph 1 and the Disclosure of the Invention on pages 3-5 of the instant specification).

Also, given the broadest reasonable interpretation of the claims and the nature of treating pemphigus, which involves a long course of therapy which aims includes immediate and subsequent to stop the eruption of new lesions, as evidenced by the Merck Manual,
the prior art teaching of treating pemphigus with anti-CD40L antibodies reads on treating and in turn, preventing pemphigus as it reads on preventing the eruption of new lesions in the long course of treatment of this disease (e.g., see pages 829-831, particularly Treatment).

Further, it is noted that the Merck Manual teaches Diagnosis of Pemphigus in order to determine the population of interest for treatment (e.g., see page 829).

It is noted that Di Padova et al. also teaches "treatment and/or prevention diseases or disorders" (e.g., see paragraph [0083]).

One of ordinary skill in the art at the time the invention was made would have been motivated to select treating patients diagnosed with pemphigus or as an ongoing treatment in order to stop the eruption of new lesions in order to prevent the pemphigus or the characteristics of pemphigus with anti-CD40L antibodies, given the teachings of the primary references as to the applicability of anti-CD40L antibodies in the treatment of pemphigus. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

"The test of obviousness is not express suggestion of the claimed invention in any or all of the references but rather what the references taken collectively would suggest to those of ordinary skill in the art presumed to be familiar with them." See In re Rosselet, 146 USPQ 183, 186 (CCPA 1965).

"There is no requirement (under 35 USC 103(a)) that the prior art contain an express suggestion to combine known elements to achieve the claimed invention. Rather, the suggestion to combine may come from the prior art, as

filtered through the knowledge of one skilled in the art." Motorola, Inc. v. Interdigital Tech. Corp., 43 USPQ2d 1481, 1489 (Fed. Cir. 1997).

An obviousness determination is not the result of a rigid formula disassociated from the consideration of the facts of a case. Indeed, the common sense of those skilled in the art demonstrates why some combinations would have been obvious where others would not. See KSR Int'l Co. v. Teleflex Inc., 550 U.S., 2007 U.S. LEXIS 4745, 2007 WL 1237837, at *12 (2007) ("The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.").

Applicant's arguments have not been found persuasive.

8. No claim is allowed.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on (571) 272-0878.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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